EDITORIAL

Preventing contrast nephropathy in catheter laboratory

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Contrast nephropathy (CN), which was recognised >50 years ago,[1] is a well-known complication in patients with chronic renal insufficiency undergoing coronary angiography or interventions.[2–4] The estimated incidence of CN after coronary angiography was around 15%.[5] In fact, CN is the third leading cause of acute renal failure in hospitalised patients.[6] Development of CN may result in residual permanent renal damage, prolong hospital stay and increase medical cost.[7] In those who have had coronary intervention but complicated with CN, the estimated rate of inhospital mortality was 25% and 1-year mortality was 55%.[3] With the increasing number of patients undergoing percutaneous coronary intervention, it is expected that the burden of such iatrogenic complications will exponentially increase and effective preventive measures are imminently necessary.

The exact pathogenesis of CN is still unclear. Several injury pathways have been proposed. The contrast agent may have direct cytotoxic effects due to relatively high tissue osmolality. The contrast medium induces renal vasoconstriction, leading to tubular injury or even necrosis. Elevated endothelin levels and other vasoconstrictor levels were detected in those with CN. Subsequent reperfusion injury may increase free radical formation and create oxidative stress. The contrast medium may precipitate with Tamm Horsfall glycoprotein in distal tubule lumen and form casts.[8] With reference to these potential mechanisms, efficacy of various prophylactic pharmacological agents—for example, antioxidants, vasodilators and so on—have been evaluated in many randomised trials, but most of them failed to show convincing benefit in preventing CN. Non-pharmacological interventions including haemodialysis and haemofiltration have also been tested. In one randomised trial testing the efficacy of the latter prophylactic measure, patients who underwent haemofiltration had a lower incidence of CN, defined as >25% increase in serum creatinine concentration.[9] However, the intervention itself may actually decrease serum creatinine concentration, and questions have been raised about the real efficacy in preventing CN by this costly procedure. A similar problem was also observed with the use of N-acetylcysteine (NAC). Ever since Tepel *et al*[10] reported that NAC may have the potential to reduce CN, there has been a blooming of randomised controlled trials using NAC as the prophylactic agent in patients requiring coronary angiography or interventions. Heterogeneous rather than consistent results were observed in these trials, including meta-analysis. Interestingly, NAC itself was also found to decrease serum creatinine concentration in healthy volunteers in one study.[11] The cystatin C concentration, a better surrogate for glomerular filtration rate (GFR), remained unchanged after NAC. What lessons can be learnt from these observations? First, one must ascertain whether there is any direct interference from or interaction between the preventive measure and evaluation of CN, which is commonly estimated by serum creatinine using the standard formula.[12] Second, the occurrence of CN or the primary endpoint in a clinical trial may preferably be defined as a more solid clinical event—for example, hospital stay, temporary dialysis or even mortality—rather than as an elevation of serum creatinine or a decline in estimated GFR. Third, the contrast agent used in various trials varied widely. For intra-arterial administration, the non-ionic isomolar contrast agent seemed to be preferred as compared with a low osmolality agent.[13] Lastly, like any cardiovascular trial, a large-scale multicentre randomised controlled trial with core laboratory is necessary to determine the real efficacy of any preventive measure, as most of the published data are from single-centre experience, which may account for the heterogeneity in results observed in NAC trials.

Trimetazidine, a long-chain 3-ketoacyl coenzyme A thiolase inhibitor, was reported to have cellular anti-ischaemic properties in inhibiting oxidative phosphorylation by shifting energy production from free fatty acid to glucose oxidation in myocardial tissue. It has been shown in various trials that the drug is beneficial in patients with angina pectoris, ischaemic or even non-ischaemic cardiomyopathy.[14] In this issue of *Heart*,[15] Onbasili *et al* reported the efficacy of trimetazidine in reducing CN in patients undergoing cardiac catheterisation. The definition of CN was an absolute increase of >5 mg/dl or a relative increase of >25% in serum creatinine within 48 h after contrast administration. There was a significantly lower incidence of CN in the treatment group, and the authors concluded that trimetazidine with saline was more effective than saline alone in preventing CN. Should we adopt this drug as one of the measures to prevent CN in our patients? The answer is not yet known. With the concerns mentioned, it is not known whether the drug has any significant interaction with serum creatinine measurement, especially given that a significant

Abbreviations: CN, contrast nephropathy; GFR, glomerular filtration rate; NAC, N-acetylcysteine

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drop in creatinine level at day 7 was observed in the treatment group. There was also no information about the clinical endpoint—for example, duration of hospitalisation—in this study. In addition, iopromide, a low-osmolality agent rather than an iso-osmolar agent, was used. Nevertheless, this report highlights the potential role of a new approach such as cytoprotective or metabolic treatment for CN prevention. Most importantly, trimetazidine is, in general, considered a safe drug without significant side effects, as in the current study. Further studies with more patients and clinically relevant primary endpoints are necessary before adopting this novel treatment as the recommended prophylactic measure for CN.

What should be done to reduce the risk of CN in our patients in the catheter laboratory these days? The simple and inexpensive method may be more important than administering various controversial agents in daily practice. Proper risk identification by estimating GFR (<60 ml/min/1.73 m^2), considering alternative non-iodine contrast imaging and early preprocedural dialysis planning in patients at risk of CN, are necessary. Discontinuation of nephrotoxic drugs—for example, non-steroidal anti-inflammatory drugs—and metformin in patients with diabetes before going to the catheter laboratory is highly recommended. Adequate periprocedural intravenous 0.9% saline hydration at the rate of 1 ml/kg/h and non-ionic iso-osmolar contrast medium should be adopted in all high-risk patients. The importance of close monitoring of renal function after contrast administration has to be emphasised in all patients at risk of CN.

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REFERENCES

1 **Alwall N**, Erlanson P, Tornberg A. This clinical course of renal failure occurring after intravenous urography and/or retrograde pyelography; casuistics of 11 cases (including 7 deaths); on indications for and risks involved in the use of contrast media, including some remarks on the risk of aspiration biopsy of the kidney. *Acta Med Scand Suppl* 955, **152**:163–73.
2 **Chertow GM**, Christiansen CL, Cleary DP. Prognostic stratification in critically ill patients with acute renal failure requiring dialysis. *Arch Intern Med* 1995;**155**:1505–11.
3 **Gruberg L**, Mehran R, Dangas G, *et al*. Acute renal failure requiring dialysis after percutaneous coronary interventions. *Cathet Cardiovasc Intervent* 2001;**52**:409–16.
4 **McCullough PA**, Wolyn R, Rocher LL, *et al*. Acute renal failure after coronary intervention: incidence, risk factors, and relationship to mortality. *Am J Med* 1997;**103**:368–75.
5 **Murphy SW**, Barrett BJ, Parfrey PS. Contrast nephropathy. *J Am Soc Nephrol* 2000;**11**:177–82.
6 **Hou SH**, Bushinsky DA, Wish JB, *et al*. Hospital-acquired renal insufficiency: a prospective study. *Am J Med* 1983;**74**:243–8.
7 **Rihal CS**, Textor SC, Grill DE, *et al*. Incidence and prognostic importance of acute renal failure after percutaneous coronary intervention. *Circulation* 2002;**105**:2259–64.
8 **Fishbane S**, Durham JH, Marzo K, *et al*. N-acetylcysteine in the prevention of radiocontrast-induced nephropathy. *J Am Soc Nephrol* 2004;**15**:251–60.
9 **Marenzi G**, Marana I, Lauri G, *et al*. The prevention of radiocontrast-agent-induced nephropathy by hemofiltration. *N Engl J Med* 2003;**349**:1333–40.
10 **Tepel M**, van der Giet M, Schwarzfeld C, *et al*. Prevention of radiographic-contrast-agent-induced reductions in renal function by acetylcysteine. *N Engl J Med* 2000;**343**:180–4.
11 **Hoffmann U**, Fischereder M, Kruger B, *et al*. The value of N-acetylcysteine in the prevention of radiocontrast agent-induced nephropathy seems questionable. *J Am Soc Nephrol* 2004;**15**:407–10.
12 **Levey AS**, Bosch JP, Lewis JB, for the Modification of Diet in Renal Disease Study Group, *et al*. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. *Ann Intern Med* 1999;**130**:461–70.
13 **Davidson C**, Stacul F, McCullough PA, Contrast medium use, *et al*. *Am J Cardiol* 2006;**98**:42K–58K.
14 **Fragasso G**, Palloshi A, Puccetti P, *et al*. A randomized clinical trial of trimetazidine, a partial free fatty acid oxidation inhibitor, in patients with heart failure. *J Am Coll Cardiol* 2006;**48**:992–8.
15 **Onbasili AO**, Yeniceriglu Y, Agaoglu P, *et al*. Trimetazidine in the prevention of contrast-induced nephropathy after coronary procedures. *Heart* 2007;**93**:698–702.

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